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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,354	10/30/2003	David James Rawson	PC25373A	1622

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EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
08/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

~ipgsstl@pfizer.com

Office Action Summary	Application No.	Applicant(s)	
	10/698,354	RAWSON, DAVID JAMES	
	Examiner	Art Unit	
	LESLIE A. ROYDS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,18,20-22 and 27-30* is/are pending in the application.

4a) Of the above claim(s) *18,28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,20-22,27 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 15, 18, 20-22 and 27-30 are presented for examination.

Applicant's Amendment filed April 30, 2009 has been received and entered into the present application.

Claims 15, 18, 20-22 and 27-30 remain pending. Claims 18 and 28-29 are withdrawn from examination pursuant to 37 C.F.R. 1.142(b), since the subject matter of said claims does not encompass the elected specie of (2S,4S)-4-(3-fluorobenzyl)-pyrrolidine-2-carboxylic acid. No claims are cancelled, amended or newly added.

Applicant's arguments, filed April 30, 2009, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 20-22, 27 and 30 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making the compound (2S,4S)-4-(3-fluorobenzyl)-pyrrolidine-2-carboxylic acid (compound of claim 27 and encompassed by the generic formula of claim 15), or the hydrochloride salt thereof (as in claim 30), does not reasonably provide enablement for the use of the same, for the reasons of record set forth at p.3-12 of the previous Office Action dated March 4, 2009, of which said reasons are hereby incorporated by reference.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that the citation to Julien is a conclusory, general statement that implicitly, if not explicitly, requires pharmaceutical data for all pharmaceutical compound claims. Applicant insists that Julien does not provide evidence showing that the skilled artisan would reasonably doubt the asserted utility and that any such evidence "must be more specific and relate to the instant claims" (p.12, Remarks). Applicant states that the example of amphetamine and methamphetamine actually supports the instant claims because both compounds, while differing in structure, are active with different activity levels. Applicant further contends that the claims are enabled as amply supported in the instant specification, such as, e.g., para.[0116], which allegedly teaches test protocols to determine the activity/relative activity of the compounds and appropriate dosage levels.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, though it is noted that Applicant has *identified* his compound as an alpha-2-delta ligand for use in treating various disorders in which the alpha-2-delta receptor is implicated, the fact remains that the instant specification fails to present any evidence, either in the form of data or scientifically sound reasoning, that would support the conclusion that the instantly claimed compounds actually do function as alpha-2-delta ligands and, therefore, would be functional for the disclosed utilities. Applicant relies upon the mechanism of action (i.e., as an alpha-2-delta ligand) underlying the purported biological activity to establish that the claimed compound would have been useful for the treatment of the various disclosed disorders in which the alpha-2-delta receptor is involved. In other words, Applicant's disclosed utility rests upon both the correlation and nexus between the particular activity of the claimed compounds as alpha-2-delta ligands and a reasonable expectation of usefulness in treating the disclosed disorders related to dysfunctions of the alpha-2-delta receptor. However, the instant specification fails to provide any disclosure pertinent to this nexus between the compound and the disclosed utilities. Though Applicant provides various compounds and methods of synthesizing each, it again remains that Applicant has failed

to demonstrate that the instantly claimed compound actually functions to achieve the disclosed therapeutic interaction with the alpha-2-delta receptor such that one of skill in the art would have thereby recognized its efficacious use in treating any one or more of the disclosed disease states.

These facts coupled with the fact that the specification also fails to present either via a working (or even prophetic) example(s) or a clear, scientifically sound explanation as to what, in fact, enables the interaction with the alpha-2-delta receptor such that the skilled artisan would have been imbued with at least a reasonable expectation of predictability of action in treating the disclosed disorders by effecting this action using the compound instantly claimed clearly supports the conclusion of a lack of enabling direction provided in the instant specification as to how to use the instantly claimed compound. This is because, absent such guidance, the experimentation required to determine if the claimed compound actually functions in the alleged manner such that it would have been expected to actually be useful for the disclosed utilities would be clearly undue for the reasons already made of record in the previous Office Action, which will not be repeated herein so as not to burden the record.

Secondly, Applicant's statement that Julien implicitly, if not explicitly, requires pharmaceutical data for all pharmaceutical compound claims is not a point well taken. Julien does not contain any statement, explicit or otherwise, directed to a need to provide pharmaceutical data for all pharmaceutical compound claims. Applicant's comment to this effect is, therefore, clearly misplaced. Furthermore, Julien was cited for its clear teaching of the requirement for specificity of receptor-drug binding such that the conformation of a chemical compound must be sufficiently tailored to the particular receptor binding site such that it is actually able to bind the receptor and exert its biological effect. The fact that Julien uses an example of amphetamine and methamphetamine to illustrate this principle, as well as the principle that receptor-drug interactions are highly specific and that seemingly simple or uncomplicated modifications to a compound result in drastically different levels of pharmacologic activity such that compounds that share significant homology would not necessarily be capable of binding the same

receptor, is immaterial because Julien still, in its broadest teaching, clearly teaches and supports the asserted unpredictability of drug-receptor binding. Moreover, Applicant's statement that this amphetamine/methamphetamine example of Julien supports the instant claims because it teaches that the two compounds have different levels of activity but are still active is also unpersuasive. While the two compounds may preserve some level of activity, the fact remains that, in order to be useful for, for example, treating a disease, the compound must exert at least a threshold level of activity that is potent enough to elicit a positive therapeutic response by the patient (i.e., treatment of the disease). Without at least this threshold level of activity, the fact that a compound may retain some minimal level of biological activity does not remedy the fact that the compound does not have enough activity to be therapeutically useful for the disclosed utilities.

Thirdly, and lastly, though Applicant contends that the specification amply enables the instant claims, the specification in its entirety has been fully and carefully considered, but again fails to establish that the instantly claimed compound actually functions in the manner disclosed (i.e., as an alpha-2-delta receptor ligand) such that it would have been reasonably expected to be useful for the disclosed utilities. While it is understood that Applicant has provided extensive disclosure of the alpha-2-delta receptor, what disorders are associated with dysfunctions of alpha-2-delta receptors, therapeutic dosages of the compounds, how the artisan can administer the disclosed compounds, etc., it is again reiterated that the missing nexus in the instant disclosure is that the instantly claimed compound can, in actuality, function as an alpha-2-delta ligand. Thus, these sections of the specification (in particular, para.[0116], which Applicant states provides test protocols for determining relative activity of the compounds, but does not, in fact, provide such disclosure regarding so-called "test protocols"), while noted, do not overcome the fact that the instantly claimed compound must still be enabled to function as an alpha-2-delta ligand, which, for the reasons *supra*, and those already of record, it is not.

For these reasons *supra*, and those previously made of record at p.3-12 of the Office Action dated March 4, 2009, rejection of claims 15, 20-22, 27 and 30 remains proper.

Conclusion

Rejection of claims 15, 20-22, 27 and 30 is proper.

Claims 18 and 28-29 are withdrawn from consideration pursuant to 37 C.F.R. 1.142(b).

No claims of the present application are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system.

Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

August 4, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614